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[Cellulose/*analogs & derivatives](#)
[Cellulose/*therapeutic use](#)
[Simian Acquired Immunodeficiency Syndrome/*prevention & control](#)
[Administration, Topical; Animal; Antiviral Agents/administration & dosage; Cellulose/administration & dosage; Disease Models, Animal; Disease Transmission/prevention & control; HIV Infections/transmission; Human; Macaca mulatta; SIV/drug effects; SIV/genetics; SIV/physiology; Simian Acquired Immunodeficiency Syndrome/transmission; Simian Acquired Immunodeficiency Syndrome/virology; Support, Non-U.S. Gov't; Vaginal Creams, Foams and Jellies](#)**Abstract:** Human immunodeficiency virus type 1 (HIV-1) infection continues to spread in developing countries, mostly through heterosexual transmission. The development of a safe and cost-effective topical microbicide, effective against a range of STDs including HIV-1, would greatly impact the ongoing epidemic. When formulated in a vehicle, a micronized form of cellulose acetate *phthalate* (CAP), which is an inactive pharmaceutical excipient, has been shown to inactivate HIV-1, herpes simplex virus types 1 and 2, cytomegalovirus, Neisseria gonorrhoeae, Trichomonas vaginalis, Haemophilus ducreyi, and Chlamydia trachomatis in vitro. Formulated CAP was also shown to be effective against herpes simplex virus type 2 in vivo. Here we show that a formulation of CAP protected four of six rhesus monkeys from vaginal infection with simian immunodeficiency virus. Thus, CAP may be a candidate for use as a topical microbicide for preventing HIV-1 infection in humans.**CAS Registry No.:** 0 (Antiviral Agents)
0 (Vaginal Creams, Foams and Jellies)
9004-34-6 (Cellulose)
9004-38-0 (cellulose acetate *phthalate*)**Entry Date(s):** *Date Created:* 20001102 *Date Completed:* 20010104**Citation ID(s):** *PMID:* 11036053 *Medline UI:* 20493142**Persistent Link to this Article:** <http://search.epnet.com/direct.asp?an=11036053&db=cmedm&tg=PM>**Database:** MEDLINEFormats: [Citation](#)

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◀ 6 of 10 ▶ [Result List](#) | [Refine Search](#) [Print](#) [E-mail](#) [Save](#) [Add to folder](#) [Folder is empty.](#)Formats: [Citation](#) [Linked Full Text](#)**Title:** Microbicide for prevention of sexually transmitted diseases using a pharmaceutical excipient.**Author(s):** Neurath AR**Author's Address:** New York Blood Center, NY, USA. neurath@nybc.org**Source:** [AIDS patient care and STDs](#) [AIDS Patient Care STDS] 2000 Apr; 14 (4), pp. 215-9.**Pub. Type:** Journal Article; Review; Review, Tutorial**Language:** English**Journal Info:** *Country of Publication:* UNITED STATES *NLM ID:* 9607225 *ISSN:* 1087-2914 *Subsets:* X**MeSH Terms:** [Anti-Infective Agents/*administration & dosage](#)
[Excipients/*administration & dosage](#)
[HIV-1/*drug effects](#)
[Sexually Transmitted Diseases/*prevention & control](#)
[Animal; Anti-Infective Agents/pharmacology; Controlled Clinical Trials; Disease Models, Animal; Excipients/pharmacology; Human; Mice; Microbial Sensitivity Tests; Treatment Outcome](#)**Abstract:** Preferred microbicides are expected to inactivate most sexually transmitted viral and nonviral pathogens, including *HIV-1*, without affecting lactobacilli, components of the natural defense system against sexually transmitted diseases (STDs), be widely available, be inexpensive, and have an established safety record for human use. We show here that cellulose acetate *phthalate* [C-A-P enteric coating polymer (Eastman)], a compound used for coating of enteric tablets, meets all these criteria.**No. of References:** 1**CAS Registry No.:** 0 (Anti-Infective Agents)
0 (Excipients)**Revision Date:** 20001218**Entry Date(s):** *Date Created:* 20000921 *Date Completed:* 20000921**Citation ID(s):** *PMID:* 10806641 *Medline UI:* 20266604**Persistent Link to this Article:** <http://search.epnet.com/direct.asp?an=10806641&db=cmedm&tg=PM>**Database:** MEDLINEFormats: [Citation](#) [Linked Full Text](#)

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Formats:  [Citation](#)  [HTML Full Text](#)  [PDF Full Text](#)

Title: 'Inactive' polymer is active against sexually transmitted diseases.

Subject(s): CELLULOSE acetate -- Therapeutic use; STABILIZING agents -- Therapeutic use; HIV infections -- Treatment; SEXUALLY transmitted diseases -- Treatment; HERPES genitalis -- Treatment

Author(s): Larkin, Marilyn

Source: Lancet, 07/31/99, Vol. 354 Issue 9176, p399, 1/3p

Abstract: States that an 'inactive' pharmaceutical excipient, cellulose acetate phthalate (CAP), is active against the HIV-1 virus, the genital herpes virus, and bacteria that causes several sexually transmitted diseases. Research by Neurath et al from the New York Blood Center in New York City; How CAP does not affect the lactobacilli found in vaginal flora.

AN: 2098796

ISSN: 0099-5355

Persistent Link to this Article: <http://search.epnet.com/direct.asp?an=2098796&db=aph>

Database: Academic Search Premier

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Section: SCIENCE AND MEDICINE

NEWS

'INACTIVE' POLYMER IS ACTIVE AGAINST SEXUALLY TRANSMITTED DISEASES.

An "inactive" pharmaceutical excipient--cellulose acetate phthalate (CAP)--used for years to make enteric coatings for pills and capsules is, in fact, quite active against the HIV-1 virus, the genital herpes virus, and bacteria that cause several common sexually transmitted diseases (STDs), report researchers from the New York Blood Center (New York City, NY, USA). "It has broad activity and an established safety record--that's the promise", says lead investigator A Robert Neurath.

Neurath and co-workers were searching for an inexpensive, widely available antimicrobial agent when they discovered CAP. When "appropriately formulated in micronised form" for application in a cream, CAP inactivated STD pathogens but did not affect the lactobacilli naturally found in the vaginal flora, which also help prevent STDs (Biologicals 1999; 27: 11-21).

Animal studies suggest CAP does not irritate the vagina and is not absorbed systemically after topical application, adds Neurath, also important qualities for a microbicide (see Lancet 1998; 351: 964).

"CAP's activity against bacterial STDs is critical", stresses Neurath, "because these are thought to predispose to HIV-1 infection. We really should avoid any new agent that is totally specific for HIV-1", he continues, "because it might not be affordable and something else would still be needed to deal with the other STDs".

CAP "is still in the very early stages of development, so it's hard to know how it's going to go", cautions Penelope Hitchcock, chief of the STD branch of the US National Institutes of Allergy and Infectious Diseases (Bethesda, MD, USA). But Neurath's work and that of other researchers is important, she says, because "it takes a lot of great ideas and potential products before you actually find the winner".

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By Marilyn Larkin

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**Abstract:** Initial biologic events that underlie sexual transmission of HIV-1 are poorly understood. To model these events, we exposed human immature Langerhans cells (LCs) within epithelial tissue explants to two primary and two laboratory-adapted HIV-1 isolates. We detected HIV-1(Ba-L) infection in single LCs that spontaneously emigrated from explants by flow cytometry (median of infected LCs = 0.52%, range = 0.08-4.77%). HIV-1-infected LCs downregulated surface CD4 and CD83, whereas MHC class II, CD80, and CD86 were unchanged. For all HIV-1 strains tested, emigrated LCs were critical in establishing high levels of infection (0.1-1 microg HIV-1 p24 per milliliter) in cocultured autologous or allogeneic T cells. HIV-1(Ba-L) (an R5 HIV-1 strain) more efficiently infected LC-T cell cocultures when compared with HIV-1(IIIB) (an X4 HIV-1 strain). Interestingly, pretreatment of explants with either aminooxypentane-RANTES (regulated upon activation, normal T cell expressed and secreted) or cellulose acetate *phthalate* (potential microbicides) blocked HIV-1 infection of LCs and subsequent T cell infection in a dose-dependent manner. In summary, we document HIV-1 infection in single LCs after exposure to virus within epithelial tissue, demonstrate that relatively low numbers of these cells are capable of inducing high levels of infection in cocultured T cells, and provide a useful explant model for testing of agents designed to block sexual transmission of HIV-1.

**CAS Registry No.:** 0 (Anti-HIV Agents)  
0 (RANTES)  
0 (aminooxypentane-RANTES)

**Entry Date(s):** *Date Created:* 20001218 *Date Completed:* 20001218**Citation ID(s):** *PMID:* 11085750 *Medline UI:* 20538493**Persistent Link to this Article:** <http://search.epnet.com/direct.asp?an=11085750&db=cmedm&tg=PM>**Database:** MEDLINEFormats: [Citation](#)

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◀ 2 of 2 ▶ [Result List](#) | [Refine Search](#) | [Print](#) | [E-mail](#) | [Save](#) | [Add to folder](#) | [Folder has items.](#)Formats: [Citation](#)**Title:** Cellulose acetate *phthalate* (CAP): an 'inactive' pharmaceutical excipient with antiviral activity in the mouse model of genital herpesvirus infection.**Author(s):** Gytoku T; Aurelian L; Neurath AR**Author's Address:** Department of Pharmacology, The University of Maryland School of Medicine, Baltimore 21201, USA.**Source:** [Antiviral chemistry & chemotherapy](#) [Antivir Chem Chemother] 1999 Nov; 10 (6), pp. 327-32.**Pub. Type:** Journal Article**Language:** English**Journal Info:** *Country of Publication:* ENGLAND *NLM ID:* 9009212 *ISSN:* 0956-3202 *Subsets:* IM**MeSH Terms:** [Antiviral Agents/\\*therapeutic use](#)  
[Cellulose/\\*analogs & derivatives](#)  
[Excipients/\\*therapeutic use](#)  
[Herpes Genitalis/\\*drug therapy](#)  
[Animal; Cellulose/therapeutic use; Cercopithecus aethiops; Disease Models,](#)  
[Animal; Female; Mice; Support, Non-U.S. Gov't; Vaginal Diseases/drug therapy; Vero Cells](#)

**Abstract:** The spread of sexually transmitted infections caused by *herpes simplex virus type 2* (HSV-2) has continued unabated. At least 20% of the United States population has been infected with HSV-2 and there is a high probability of further virus transmission by asymptomatic carriers. Given the absence of effective vaccines, this indicates the need to develop prophylactic measures such as topical microbicides that have antiviral activity. Recent studies indicate that cellulose acetate *phthalate* (CAP), an inactive pharmaceutical excipient commonly used in the production of enteric tablets and capsules, is a broad specificity microbicide against diverse sexually transmitted pathogens. When appropriately formulated in micronized form, it inactivates various viruses, including HSV-2, in vitro. Here we show that CAP inhibits HSV-2 infection in the mouse model of genital HSV-2 infection. Pretreatment with micronized CAP formulated in a glycerol-based cream with colloidal silicone dioxide significantly reduced the proportion of HSV-2-infected mice (10% virus shedding, 0-5% lesion development and 0% fatality for CAP as compared to 84% shedding, 63% lesion development and 63% fatality in saline-treated mice). These differences were significant ( $P < \text{or} = 0.0002$  by the test of equality of two proportions). Virus titres in the minority of mice that developed infection were similar to those in untreated mice. HSV-2 infection was not inhibited by treatment with CAP formulated with other inactive ingredients (for example povidone plus crospovidone) instead of silicone dioxide, presumably reflecting CAP complexation/inactivation. These data suggest that properly formulated, CAP may be an efficacious agent for preventing vaginal transmission of genital herpesvirus infections.

**CAS Registry No.:** 0 (Antiviral Agents)  
0 (Excipients)  
9004-34-6 (Cellulose)  
9004-38-0 (cellulose acetate *phthalate*)**Revision Date:** 20001218**Entry Date(s):** *Date Created:* 20000127 *Date Completed:* 20000127**Citation ID(s):** *PMID:* 10628808 *Medline UI:* 20092430**Persistent Link to this Article:** <http://search.epnet.com/direct.asp?an=10628808&db=cmedm&tg=PM>**Database:** MEDLINE

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Cellulose/\*analogs & derivatives  
Cellulose/\*therapeutic use  
Simian Acquired Immunodeficiency Syndrome/\*prevention & control  
Administration, Topical; Animal; Antiviral Agents/administration &  
dosage; Cellulose/administration & dosage; Disease Models, Animal; Disease  
Transmission/prevention & control; HIV Infections/transmission; Human; Macaca  
mulatta; SIV/drug effects; SIV/genetics; SIV/physiology; Simian Acquired Immunodeficiency  
Syndrome/transmission; Simian Acquired Immunodeficiency Syndrome/virology; Support,  
Non-U.S. Gov't; Vaginal Creams, Foams and Jellies**Abstract:** Human immunodeficiency virus type 1 (HIV-1) infection continues to spread in developing countries, mostly through heterosexual transmission. The development of a safe and cost-effective topical microbicide, effective against a range of STDs including HIV-1, would greatly impact the ongoing epidemic. When formulated in a vehicle, a micronized form of cellulose acetate *phthalate* (CAP), which is an inactive pharmaceutical excipient, has been shown to inactivate HIV-1, *herpes simplex virus* types 1 and 2, cytomegalovirus, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, *Haemophilus ducreyi*, and *Chlamydia trachomatis* in vitro. Formulated CAP was also shown to be effective against *herpes simplex virus* type 2 in vivo. Here we show that a formulation of CAP protected four of six rhesus monkeys from vaginal infection with simian immunodeficiency virus. Thus, CAP may be a candidate for use as a topical microbicide for preventing HIV-1 infection in humans.**CAS Registry No.:** 0 (Antiviral Agents)  
0 (Vaginal Creams, Foams and Jellies)  
9004-34-6 (Cellulose)  
9004-38-0 (cellulose acetate *phthalate*)**Entry Date(s):** *Date Created:* 20001102 *Date Completed:* 20010104**Citation ID(s):** *PMID:* 11036053 *Medline UI:* 20493142**Persistent Link to this Article:** <http://search.epnet.com/direct.asp?an=11036053&db=cmedm&tg=PM>**Database:** MEDLINEFormats: [Citation](#)

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[Oligopeptides/\\*pharmacokinetics](#)  
[Administration, Oral](#); [Animal](#); [Biological Availability](#); [Comparative Study](#); [Dogs](#); [Rats](#); [Species Specificity](#)

**Abstract:** The bioavailability (BA) of a tripeptide protease inhibitor, KNI-272, which has a strong pharmacological potential for treating human immunodeficiency virus type 1 (*HIV-1*), has been studied in beagle dogs by administering several oral dosage forms. The tested dosage forms were form 1, plain gelatin capsules; forms 2 and 3, gelatin capsules of which the inner and outer surfaces were coated with 7G ethylcellulose (EC, 30  $\mu$ m thickness) and an enteric coating material, hydroxypropyl methylcellulose *phthalate* (HP-55), respectively; and form 4, gelatin capsules of which the inner surface is coated with 10G EC (60  $\mu$ m thickness). The difference between forms 2 and 3 was the amount of citric acid contained in the capsule, namely 100 mg in form 2 and 200 mg in form 3. One hundred milligrams of KNI-272 was placed in each capsule after being dissolved with propylene glycol (PG). These capsules were used to deliver KNI-272 to the stomach for form 1, to the upper part of the small intestine for forms 2 and 3, and to the middle part of the small intestine for form 4. As a reference, 50.0 mg of KNI-272 was administered to the same dogs by intravenous (IV) infusion for 15 min. By measuring the plasma drug levels with the HPLC method, BAs were estimated for each test dosage form. Form 1 showed the highest BA of 26 center dot 2  $\pm$  7 center dot 0% (mean  $\pm$  SE), though the other capsules showed BAs of approximately 10%, namely 6 center dot 6  $\pm$  0 center dot 4% for form 2, 10 center dot 3  $\pm$  1 center dot 1% for form 3 and 14 center dot 2  $\pm$  1 center dot 0% for form 4. Therefore, as the site where KNI-272 is released from the capsule becomes higher, the BA increases. In addition, as the amount of citric acid contained in a capsule increases, the BA value tends to increase. These results suggest that KNI-272 is stable and not extensively hydrolysed in the gut after oral administration, that the dissolution process into GI fluids is important for the BA of KNI-272, and that the most appropriate absorption site of KNI-272 in dogs is the duodenum. The potential of this new tripeptide compound as an orally active anti-AIDS drug has been confirmed.

**CAS Registry No.:** 0 (*HIV* Protease Inhibitors)  
0 (Oligopeptides)  
147318-81-8 (kynostatin 272)**Revision Date:** 20011113**Entry Date(s):** *Date Created:* 19970311 *Date Completed:* 19970311**Citation ID(s):** *PMID:* 8907719 *Medline UI:* 97063852**Persistent Link to this Article:** <http://search.epnet.com/direct.asp?an=8907719&db=cmedm&tg=PM>**Database:** MEDLINE

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**Title:** Anti-tumor promoting action of phthalic acid mono-n-butyl ester cupric salt, a biomimetic superoxide dismutase.

**Author(s):** Yamamoto S; Nakadate T; Aizu E; Kato R

**Author's Address:** Department of Pharmacology, School of Medicine, Keio University, Tokyo, Japan.

**Source:** *Carcinogenesis* [Carcinogenesis] 1990 May; 11 (5), pp. 749-54.

**Pub. Type:** Journal Article

**Language:** English

**Journal Info:** *Country of Publication:* UNITED STATES *NLM ID:* 8008055 *ISSN:* 0143-3334 *Subsets:* IM

**MeSH Terms:** [Antineoplastic Agents/\\*pharmacology](#)  
[Dibutyl Phthalate/\\*pharmacology](#)  
[Phthalic Acids/\\*pharmacology](#)  
[9,10-Dimethyl-1,2-benzanthracene; Administration, Topical; Animal; Benzanthraces/adverse effects; Cells, Cultured; Dermatitis, Contact/etiology; Ear Diseases/chemically induced; Edema/chemically induced; Enzyme Induction; Epidermis/cytology; Epidermis/drug effects; Female; Mice; Ornithine Decarboxylase/metabolism; Papilloma/chemically induced; Skin Neoplasms/chemically induced; Superoxide Dismutase/metabolism; Support, Non-U.S. Gov't; Tetradecanoylphorbol Acetate/administration & dosage](#)

**Abstract:** Skin tumor promotion induced by 12-O-tetradecanoylphorbol-13-acetate (TPA) was inhibited by a concurrent and topical application of phthalic acid mono-n-butyl ester cupric salt (PAMBCu) in CD-1 mice initiated with 7,12-dimethylbenz[a]anthracene. PAMBCu inhibited TPA-caused epidermal ornithine decarboxylase (ODC) induction and ear edema formation, i.e. skin inflammation. However, neither PAMBCu nor superoxide dismutase (SOD) inhibited TPA-caused ODC induction in primary cultured mouse epidermal cells. 7-Bromomethylbenz[a]anthracene (BrMBA) is known to be a non-TPA type of tumor promoting agent. Epidermal ODC induction and inflammation caused by BrMBA were not inhibited by a concurrent application of PAMBCu. When mice were topically treated twice with PAMBCu, i.e. concurrently with and 7 h after BrMBA treatment, BrMBA-caused ODC induction was markedly suppressed. The same dose regimen of PAMBCu, however, failed to inhibit tumor promotion and inflammation caused by BrMBA. PAMBCu showed SOD-mimetic activity in superoxide generating systems, i.e. xanthine-xanthine oxidase reaction and TPA-stimulated polymorphonuclear leukocytes (PMN). Mono-n-butyl *phthalate*, which lacks SOD-mimetic activity, failed to inhibit TPA-caused ODC induction and skin inflammation. Therefore, inhibition by PAMBCu of TPA-caused tumor promotion, epidermal ODC induction and inflammation may be attributable to its SOD-mimetic activity. The results also support the contention that a superoxide anion of non-epidermal cell origin, such as PMN and macrophages, plays a role (probably some enhancing role) in in vivo ODC induction and tumor promotion caused by TPA. Failure of PAMBCu to inhibit BrMBA-caused tumor promotion suggests that superoxide anion generation is not involved in the tumor promoting action of this agent and that the anti-tumor promoting action of PAMBCu is dependent on the nature of the tumor promoting agents.

**CAS Registry No.:** 0 (Antineoplastic Agents)  
0 (Benzanthracenes)  
0 (Phthalic Acids)  
16561-29-8 (Tetradecanoylphorbol Acetate)  
24961-39-5 (7-bromomethylbenzanthraces)  
57-97-6 (9,10-Dimethyl-1,2-benzanthracene)  
84-74-2 (Dibutyl *Phthalate*)  
EC 1.15.1.1 (Superoxide Dismutase)  
EC 4.1.1.17 (Ornithine Decarboxylase)





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**Title:** Design of a 'microbicide' for prevention of sexually transmitted diseases using 'inactive' pharmaceutical excipients.

**Author(s):** Neurath AR; Strick N; Li YY; Lin K; Jiang S

**Author's Address:** The New York Blood Center, 310 E. 67th St, New York, NY, 10021, USA.

**Source:** Biologicals : journal of the International Association of Biological Standardization [Biologicals]  
1999 Mar; 27 (1), pp. 11-21.

**Pub. Type:** Journal Article

**Language:** English

**Journal Info:** *Country of Publication:* ENGLAND *NLM ID:* 9004494 *ISSN:* 1045-1056 *Subsets:* IM; X

**MeSH Terms:** Anti-Infective Agents/\*pharmacology  
Cellulose/\*analogs & derivatives  
Excipients/\*pharmacology  
Sexually Transmitted Diseases/\*prevention & control  
Animal; Cell Line; Cellulose/pharmacology; Chlamydia trachomatis/drug effects; Drug  
Evaluation, Preclinical; HIV Infections/prevention & control; HIV-1/drug effects; Haemophilus  
ducreyi/drug effects; Herpesvirus 1, Human/drug effects; Herpesvirus 2, Human/drug  
effects; Human; Lactobacillus/drug effects; Methylcellulose/analogs &  
derivatives; Methylcellulose/pharmacology; Microbial Sensitivity Tests; Neisseria  
gonorrhoeae/drug effects; Trichomonas vaginalis/drug effects

**Abstract:** The human immunodeficiency virus (HIV-1) pandemic has been driven primarily by the sexual transmission of the virus, and facilitated by prior infections with other sexually transmitted disease (STD) pathogens. Although treatment of these STDs has been proposed as a means to decrease the rate of HIV-1 sexual transmission, preventive measures effective against both HIV-1 and other STD pathogens are expected to have a larger impact. These measures include topically applied mechanical and chemical (i.e. microbicidal) barriers. Microbicides of preference should have a broad specificity against diverse STD pathogens and a well established safety record, considering their repeated use over decades. Here, we report that cellulose acetate *phthalate* (CAP), an "inactive" pharmaceutical excipient, commonly used in the production of enteric tablets and capsules: (1) has antiviral activity against HIV-1 and several herpesviruses (HSV); and (2) when appropriately formulated, in micronized form, inactivates HIV-1, HSV-1, HSV-2, cytomegalovirus, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, *Haemophilus ducreyi* and *Chlamydia trachomatis* but does not affect *Lactobacilli*, components of the natural vaginal flora contributing to resistance against STDs. Thus, the CAP formulations meet the criteria for preferred microbicides and warrant further evaluation in vivo in humans. (Copyright 1999 The International Association for Biologicals.)

**CAS Registry No.:** 0 (Anti-Infective Agents)  
0 (Excipients)  
9004-34-6 (Cellulose)  
9004-38-0 (cellulose acetate *phthalate*)  
9004-67-5 (Methylcellulose)  
9050-31-1 (hydroxypropyl methylcellulose *phthalate*)

**Revision Date:** 20011113

**Entry Date(s):** *Date Created:* 19990908 *Date Completed:* 19990908

**Citation ID(s):** *PMID:* 10441398 *Medline UI:* 99373203

**Persistent Link to this Article:** <http://search.epnet.com/direct.asp?an=10441398&db=cmedm&tg=PM>